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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/787,138	SCHLESSINGER ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/27/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-13 are pending.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number. The following phrase recited on the first page of the instant Specification: "The present application is related to US Application Serial Number 08/357,642", does not define a specific relationship between the instant Specification/Application and the prior Application.

The Instant application is claiming the benefit of a prior filed nonprovisional application under 35 U.S.C. 120, 121, or 365(c). Copendency between the current application and the prior application is required. Application 08/357,642 matured into US Patent on November 17, 1998. Application serial number 09/476,484 was filed on December 30, 1999. There is no copendency between the instant Application, Application serial number 09/476,484 and Application 08/357,642. Priority back to the filing date of December 15, 1994 is not possible in the instant Application as copendency between Applications was broken when Application 08/357,642 issued into US Patent 5,837,524 on November 17, 1998.

Information Disclosure Statement

1. The information disclosure statement filed February 27, 2004 has been considered.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1 (Method of identifying/screening) , 8 and 11 (Method of diagnosis) of this application conflict with claims 11-12, respectively of Application No. 10/292,524. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

4. Claims 1-7 of this application conflict with claims 16-34 of Application No. US 10/464,805. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may

be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

5. Claims 1, 3, 5-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 9-10 of U.S. Patent No. 6,689,806. Although the conflicting claims are not identical, they are not patentably distinct from each other because the allowed method utilizes a species of compound define as a species of indolinone compound, and the instantly claimed method utilizes a genus of indolinone compounds in a method of modulating serine protein kinase activity (see '806, claim 15) which is within the definition of PYK2 of the instant Specification (see Instant specification page 2, paragraph 2 "Raf " and "CAK" and "CAD" and page 9, paragraph 5, "phosphorylation of a natural binding partner on tyrosine, threonine or serine residues"// US Pat. 6,689,806, col. 52, lines 64-67 and col. 53, line 12). The instant claims recite the term "assaying" and the allowed claim recites "contacting"; these are analogous terms. The instantly claimed genus of methods is anticipated by the allowed species.

6. Claims 1, 3, 5-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-8,13-14 of U.S. Patent No. 6,680,335. Although the conflicting claims are not identical, they are not patentably distinct from each other because the allowed method utilizes a species of compound define as a species of indolinone

compound defined in claim 1 of US Pat. 6,680,335, and the instantly claimed method utilizes a genus of indolinone compounds in a method of modulating of serine protein kinase activity (see US Pat. 6,680,335 claim 13-14) which is within the definition of PYK2 of the instant Specification (see Instant specification page 2, paragraph 2 "Raf " and "CAK" and "CAD" and page 9, paragraph 5, "phosphorylation of a natural binding partner on tyrosine, threonine or serine residues"; US Pat. 6,680,335, claim 15). The instantly claimed genus of methods is anticipated by the allowed species.

7. Claims 1, 3, 5-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 18-19 of U.S. Patent No. 6,514,981. Although the conflicting claims are not identical, they are not patentably distinct from each other because the allowed method utilizes a species of compound define as a species of indolinone compound, and the instantly claimed method utilizes a genus of indolinone compounds in a method of modulating protein kinase activity (see '981, claims 18-19) which is within the definition of PYK2 of the instant Specification (see Instant specification page 2, paragraph 3" PKY2 is a non-receptor tyrosine kinase"// US Pat. . 6,514,981 "col. 50, lines 6-10). The instantly claimed genus of methods is anticipated by the allowed species.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps and for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. and a gap between the steps. See MPEP § 2172.01. The omitted steps and elements are:

10. Claims 1-7 recite the methods step of "assaying one or more compounds for those able to modulate said interaction as a means to identify said potentially useful compounds". The modulation is not determined relative to any specific reference point, either positive or negative control, to determine if modulation has taken place. An increase in the interaction of PYK2 polypeptide and a natural binding partner can not be determined as no starting point is defined. A decrease in the interaction between also can not be PYK2 polypeptide and a natural binding partner can not be determined based upon the single methods step of "assaying one or more compounds". No means for identification of any type of interaction, no less modulation, is positively recited in the claims. Essential elements to determine modulation, and methods steps which recite essential steps to determine modulation are missing. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed relative to what is being assayed to determine an interaction, and whether or not the compound modulates the interaction.

Claims 8-13 recite the methods step of "detecting a change in the interaction". What is provided, reacted and measured to determine a change in the interaction is not recited in the claim. Essential elements for carrying out the method of diagnosing any type of disease or

disorder is missing from the claim. No point of reference for change is determined, so how a change can be detected is not distinctly claimed. The claimed methods step only defines an indication, but the preamble requires diagnosis; the recited methods step does not positively correlate with the recited intended use of the claimed method. Natural changes in kinase levels are not taken into consideration, in detecting a change in the interaction. The source of the interaction is not defined to be normal or abnormal, therefore the detecting need not be indicative of anything as what is detected does not correlate with anything. *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-5,7-8, and 9-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Sugen, WO96/18738 (Reference cited in Applicant's USPTO-1449).

(Instant claim 1) Sugen discloses the instantly claimed invention directed to a:

method of identifying compounds potentially useful to treat or to prevent diseases or disorder (see page 16, lines 10-17, "screening potential agents useful for treatment of a disease or condition"),

wherein the disease or disorder is characterized by an inflammatory response (see page 16, lines 31-37; page 17, lines 1-14; page52, lines 25-32: which list conditions that are associated

with an inflammatory response) involving an abnormality in a signal transduction pathway (see abstract, front page "a disease or condition characterized by an abnormality in a signal transduction pathway") that includes an interaction (see page 16, lines 10-17) between a PYK2 polypeptide and a natural binding partner (NBP) (see page 7, lines 2-27 defines binding partners for PYK2) the method, comprising the step of :

assaying one or more compounds for those able to modulate(see page 56, line 1-5, inhibiting or promoting the interaction between components of the complexes (e.g. PYK2:NBP complexes; see page 72, section XVI, lines 25-36, page 73, lines 1-36), said interaction as a means to identify said potentially useful compounds (see page 16, line 15 "assaying potential agents" and page 16, lines 3-9).

(Instant claim 2): the inflammatory condition being associated with inflammatory bowel diseases (the reference teaches the detection of agents that block or promote interaction (modulators) through evaluation of intestinal cell (see page 25, line 27) and GI-tract cells (see page 25, line 27) which would identify potentially useful compounds able to modulate inflammatory bowel disease as the method utilizes cells associated with the bowel. Claim 2 also recites the limitation "connective tissue disease". The recited intended use of the method of identifying compounds, does not define over the applied prior art, which carries out the positively recited methods step of claim 1 from which claim 2 depends. Claim 2 seeks to modify the preamble of the method, but the methods step is the same as that of claim 1 which identifies a compound able to modulate the interaction of PYK2 with its natural binding partner (NBP).

(Instant claim 3): *in vitro (*see page 77, line 10; page 25, line 16 "in vitro for therapy or diagnosis"; page 15, lines 36-37 and page 16, lines 1-2 "incubating the compound with a PYK2 polypeptide", wherein see page 16 lines 3-9, "the compound inhibits a phosphoryation activity of PYK2"; see page 74, lines 34-37 and page 75, lines 1-37 and page 76).

(Instant claim 4): *in vivo* (see page 77, line 10; page 25, line 16 "in vitro for therapy or diagnosis; page 16, lines 18-22, "By "screening" is meant investigating an organism for the presence or absence of a property " and includes "measuring or detecting various properties including the level of signal transduction and the level of interaction between PYK2 polypeptide and a NBP"; and the use of "animals", see page 6, line 3)

(Instant claim 5) specifically assaying compounds that inhibit phosphorylation activity of PYK2, to include "tyrphostins, quinazolines, quinaxolines and quinolines").

(Instant claim 7): wherein the interaction is: PYK2 phosphorylation (see page 7, lines 12-21; page 7, lines 22-30),

PYK2 to phosphorylate RAK (a natural binding partner, see page 165, line 16 "promotes" interaction),

PYK2 and a natural binding partner complex formation (see page 56, section XI, lines 15-35 and lines 1-13; page 25 lines 1-20 "a peptide which blocks or promotes interaction of the PYK2 polypeptide and NBP"),

De-phosphorylation (see page 55, lines 20-33, specifically line 32 "inhibit or decrease the dephosphorylating activity"); Reversible phosphorylation of certain proteins (see page 3, lines 4-5 and 6-36; "disrupt the interaction" see page 16, lines 16-17 and page 7, line 22 "Activated PYK2 phophorylates RAK" and page 7, line 15-16 "PYK2 enzymatic activity is positively regulated by phosphorylation on tyrosine") the disruption of the interaction between RAK and PYK2 would be the result of dephophorylation, as interaction between RAK and PYK2 is contingent upon the presence of phosphate added to RAK.

PYK2 de-phosphorylation (see page 25, lines 6-10, The agent is preferably a peptide which blocks or promotes interaction of the PYK2 polypeptide and the NBP), wherein binding of PYK2 to its' natural binding partner is contingent upon phosphorylation (see page 7, lines 12-21, especially lines 14-15 "PYK2 enzymatic activity is positively regulated by phosphorylation on tyrosine) and (see page 16, lines 3-9 "In preferred embodiments, the compound inhibits a phosphylation activity of PYK2). PYK2 cannot transfer a phosphate to RAK if it lacks the phosphate through the agent compound inhibiting PYK2 activation through removal of phosphate from PYK2, thus deactivating PYK2.

(Instant claim 8) A method for diagnosis of a disease or disorder (see page 23, lines 24-30), comprising the step of :

> detecting a change in the interaction between PYK2 polypeptide and a natural binding partner, the change being indicative of a disease or disorder (see page 88, section XIX, lines 33-36 and page 89, paragraph 1, "an abnormal quantity of the complex" is compared with a normal range).

(Instant claims 9-11) recite various intended uses of the claimed method, but do not obtain a sample, or correlate with the presence or absence of disease, but only measure any level of change in the interaction of PYK2 polypeptide and a natural binding partner. In light of the fact that Sugen does disclose a method that detects an abnormal level of interaction, the reference anticipates the instantly claimed methods as the methods step claimed is disclosed by Sugen (see cited portions of Sugen immediately below that teach the measurement of abnormal levels of interaction).

(Instant claim 12) : wherein the interaction (see page 89, lines 10-37) is
PYK2 and a natural binding partner complex formation (see page 89, lines 10-37; "abnormal level of interaction "see page 24, lines 4-10) .

(Instant claim 13) wherein the change is an increase or decrease in said interaction (see page 18, lines 19-20).

13. Claims 1-7 are rejected under 35 U.S.C. 102(e, filing date June 7, 1995) as being anticipated Tang et al (US Pat. 5,880,141).

14. Tang et al discloses the instantly claimed invention directed to a:
(instant claim 1) method of identifying compounds potentially useful to treat or to prevent disease or disorder through identifying modulators of non-receptor kinase inhibitors (see US Pat. 5,880,141, col. 2, lines 58-63), the method, comprising the step of :

assaying (see '141, col. 7, lines 47-54 "a compound is subjected to a series of screens to determine the compounds ability to modulate, regulate and/or inhibit cell proliferation. These screens, in the order in which the are conducted, include biochemical assays, cell growth assays and in vivo experiments"; col. 15, lines 4-9) one or more compounds (see '141, col. 3, lines 10-33) for the ability to modulate the interaction between components of the complexes (e.g. Tyrosine kinases are non-receptor-type enzymes and are included within the scope of the instantly claimed invention at page 2, paragraph 3),

(Instant claim 2): connective tissue disease (see col. 4, line 36 "arthritis"; col. 8, line 3 "destroy cartilage")

(Instant claim 3): *in vitro (*see col. 3, line 9 "ELISA type assays in microtitre plates")

(Instant claim 4): in vivo (see col. 7, line 54)

(Instant claims 5-6): quinolones (see col. 3, line 16); quinazoloines (see col. 3, line 19-20); indolinones (see Example 5, sections 5.1-5.6)

(Instant claim 7): inhibition of formation of a complex with a natural binding partner (see brief summary text paragraph 23) "Such a composition is believed to modulate signal transduction by a tyrosine kinase, either by inhibition of catalytic activity, affinity to ATP or ability to interact with a substrate."

Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer.

"The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art".

15. Claims 1, 3 and 7 are rejected under 35 U.S.C. 102(e, filing date July 1994) as being anticipated Hirth et al.

16. Hirth et al discloses the instantly claimed invention directed to a:

(instant claim 1) method of identifying compounds potentially useful to treat or to prevent disease or disorder (in vitro binding assays, abstract), the method, comprising the step of :

assaying one or more compounds (see '198, col. 5, lines 24-35; lines 46-47, lines 61-64) for the ability to modulate the interaction between components of the complexes

(e.g. Tyrosine kinases can also be cytoplasmic, non-receptor-type enzymes and act as a downstream component of a signal transduction pathway (see '198, col. 1, lines 32-35), and are included within the scope of the instantly claimed invention at page 2, paragraph 3),

(Instant claim 3): *in vitro (*see col. 3, line 9 "ELISA type assays in microtitre plates")

(Instant claim 7): wherein the interaction is : dephosphorylation or phophorylation of tyrosine that has changed relative to an untreated control (see col. 20, claims 20- 22).

Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a

previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. "The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art".

Conclusion

17. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

18. Bourne (1995) is cited to show molecular switches associated with PYK2 complex formation.

19. Lev et al (August 1995) is cited to show PYK2 involved in regulation of ion channel and MAP kinase functions.

20. Lev et al (PG-Pub 2004/0005648) is cited to show PYK2 related products and methods.

21. Liu et al is cited to show RAFTK in Kaposi's sarcoma cells (1997).

22. Samson et al (US Pat. 6,800447) is cited to show a method of identifying compounds that will bind to CCR5 chemokine receptors.

23. Zhang et al (1998) is cited to show compounds that modulate PYK2 family members to produce enhanced tyrosine phosphorylation.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
February 1, 2005

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